UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,316	03/01/2004	Vikram Shakkottai	52044/CAB/R2682	1813

23363 7590 09/09/2005

CHRISTIE, PARKER & HALE, LLP
PO BOX 7068
PASADENA, CA 91109-7068

EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/791,316	SHAKKOTTAI ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S00

DETAILED ACTION

This Application, filed March 1, 2004, claims priority to U.S. Provisional Application 60/451,381, filed February 28, 2003.

Claims 1-27 are under consideration.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the citizenship of each inventor. The citizenship of the third inventor, Frank LaFerla, is missing.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a transgenic mouse whose genome comprises a transgene construct comprising a nucleic acid sequence encoding human small conductance calcium-activated

potassium (SK) channel protein, splice variant B1 ("SK3-1B") operably linked to a Thy1.2-SX promoter and whose genetic background is CB6F1, wherein the transgenic mouse exhibits ataxia, intention tremor, and hyperexcitable activity,

does not reasonably provide enablement for

a transgenic mouse whose genome comprises a transgene construct comprising a nucleic acid sequence encoding human small conductance calcium-activated potassium (SK) channel protein, splice variant B1 ("SK3-1B") operably linked to any neuron specific promoter, wherein the transgenic mouse exhibits ataxia, intention tremor, and hyperexcitable activity.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of

experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claimed invention broadly encompasses transgenic mice in any genetic background. The art teaches that there is unpredictability generating transgenic mice with a specific phenotype as the genetic background of the animal affects the phenotype that is exhibited by the animal model. Carlson et al. (1997, Human Molecular Genetics, 6: 1951-1959) teach that overexpression of Alzheimer amyloid precursor protein (APP) produces dramatically different phenotypes in transgenic mice depending on the genetic background (Carlson et al., abstract). Carlson et al. teach that the Tg2576 transgene array was to be transferred onto the B6 inbred background to avoid the problems inherent with outbred mice. However, it became apparent that that the proportion of mice dying prematurely increased as the percentage of B6-derived alleles increased (Carlson et al, page 1952, 1st col., 1st parag. under "The phenotypes produced by amyloid plaque-producing concentrations of APP change with genetic background", also Table 1). Carlson et al. also teach that when the APP transgene was overexpressed in inbred FVB mice, premature death was usually preceded by a variety of neurologic signs (Carlson et al., page 1952, 1st col., 2nd parag. under "The phenotypes produced by amyloid plaque-producing concentrations of APP change with genetic background" to 2nd col., 1st parag.). With respect to the instant invention,

Carlson et al.'s teachings indicate that an artisan cannot predict that overexpression of human SK3-1B would necessarily result in ataxia, intention tremor, and hyperexcitable behavior in all strains of mice. Therefore, while the specification discloses that the claimed mice exhibit ataxia, intention tremor, and hyperexcitable behavior, nothing in the art or the specification provides guidance such that an artisan would know that the phenotype was solely a result of gene overexpression and not partly influenced by genetic background. Thus, the claimed invention is limited to transgenic mice comprising CB6F1 genetic background.

The claimed invention is broad for the use of any neuron-specific promoter. The specification teaches that the Thy1.2-SX promoter was used to drive expression of SK3-1B (specification, page 2, lines 24-27). The art teaches that not all neuron-specific promoters behave similarly. That is, not all neuron-specific promoters express in neurons of all types of neural tissues and not all drive expression similarly. For example, Gloster et al. (1994, J. of Neurosci., 14: 7319-7330) teach that most neurons in the adult brain, spinal cord, and peripheral ganglia of transgenic mice comprising a transgene construct comprised of lacZ operably linked to the Tα1α–tubulin promoter did not stain with beta-galactosidase (Gloster et al., page 7325, 1st col., and Fig. 6). Vanselow et al. (1994, J. of Neurosci., 14: 499-510) teach that transgenic mice comprising a transgene construct comprising a lacZ operably linked to a GAP-43 promoter express the transgene at lower levels in neurons of adult central nervous system tissue versus in neurons of nervous system tissue of postnatal mice (Vanselow et al., page 506, Table 1). With regards to the issue of levels of transgene expression,

this variability in transgene expression amongst neuron-specific promoters raises the issue of whether enough transgene (i.e. SK3-1B) is expressed in tissue of transgenic mice such that a phenotype is seen. This issue is coupled with the fact that the art teaches that SK3-1B is a naturally occurring transcript that is present in normal human brain at about 15-60% of the level of native full-length SK3 mRNA (Tomita et al. 2003, Molecular Psychiatry, 8: 524-535, see IDS, page 525, 1st col., 2nd parag.). It is unclear at the moment what neuron-specific promoters drive expression in neurons such that the expression of SK3-1B is at levels high enough to induce a phenotype in the transgenic mouse. With regards to the issue of driving expression in neurons of specific regions of the central nervous system, Gloster et al. teach that while the Tα1α–tubulin promoter is active in neurons of embryonic tissue, they demonstrate that the Tα1α–tubulin promoter is not active in many neurons of adult tissue. It is unclear whether the lack of expression of transgenic SK3-B1 in adult tissue will result in a mouse that exhibits ataxia, intention tremors, and hyperexcitable behavior at the 7th or 8th week of life, as exhibited by the mice of the instant invention. Further, neither the specification nor the art provide any guidance as to how to select a neuron-specific promoter that expresses at levels SK3-1B wherein ataxia, intentional tremor, and hyperexcitable behavior are exhibited by the mice. Rather, based on the lack of guidance as to how to select a neuron-specific promoter, an artisan would need to empirically determine which promoters are suitable. Therefore, while the specification provides guidance on making a mouse comprising the Thy1.2-SX promoter, the

specification and the art do not enable an artisan for the broad scope of any neuron-specific promoter.

In view of the state of the art of making and using transgenic mice, the high degree of unpredictability in correlating overexpression of a gene with a particular phenotype, lack of guidance, and working examples, it would have required undue experimentation to make and/or use the invention as claimed.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER